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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/719,340	04/13/2001	John C. Kappes	30908.04.US	7175

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EXAMINER	
FOLEY, SHANON A	18

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 03/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/719,340	KAPPES ET AL.	
	Examiner	Art Unit	
	Shanon Foley	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 January 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37-86* is/are pending in the application.

4a) Of the above claim(s) *50-64 and 66-86* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37-49 and 65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

In paper no. 17, applicant amended claims 39, 43 and 48. Claims 37-86 are pending, claims 50-64, 66-86 are withdrawn from consideration and claims 37-49 and 65 are under consideration.

Election/Restrictions

This application contains claims 50-64 and 66-86, drawn to an invention nonelected with traverse in Paper No. 12. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 38 and 43-49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for reasons of record.

In response to the rejection of claim 38, applicant refers to the claim as "amended", however, the only claim 38 present in the case is recited for the first time in the preliminary amendment (paper no. 7). If there has been an amendment to the claim, applicant is requested to re-submit it, as a subsequent amendment to the claim has not been made of record.

Applicant states that the specification describes modification of a HeLa cell to express a marker gene and CCR5, CXCR4, and CD4 receptors on pages 7-9 and 13-16. Applicant argues that in view of the modifications taught in the specification, the skilled artisan would be able to ascertain what is circumscribed by claim 38.

Applicant's arguments and a review of the pages in the specification pointed to by applicant have been carefully considered. However, it is maintained that the word "originates" creates confusion. "Originates" means a point of origin giving rise to something else. From applicant's discussion, it is evident that the intent of the claim is a HeLa cell expressing receptors that HeLa cells do not normally express. However, how a cell "originates" from a HeLa cell is not clear because the point of difference between the cell of claim 38 and HeLa cells is not limited to expression of recombinant receptors. As discussed in the previous Office action, it is unclear what characteristics the cell originating from HeLa has in common with HeLa cells. To obviate this rejection, it is suggested that applicant replace "originates from" to "is a" in the claim.

With respect to claims 43 and 45, applicant argues that claim 43 does not recite that it must be known that the composition comprises at least one HIV virus. Applicant states that the method will detect virus only if it is present.

Applicant's argument has been considered, but is found unpersuasive because claim 43 recites, "a composition comprising at least one HIV virus". Therefore, the claim does not recite what applicant intends because the composition definitely comprises at least one HIV. Therefore, it is maintained that the purpose of the method remains unclear. (It is noted that applicant emphasizes that the composition of claim 43 comprises at least one HIV on page 6 of the response. It is unclear to the examiner how the composition may not comprise virus in response to the rejections under § 112, second, but does comprise virus in response to the rejection under § 112, first paragraph.)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 43-49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for detecting virus particles, does not reasonably provide enablement for detecting one HIV virus. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims for reasons of record.

Applicant argues that the scope of claim 43 is not limited to detecting only one HIV and that there is no requirement that every embodiment within the scope of a claim be enabled. Applicant asserts the instant method is a sensitive assay used to detect low viral titers and that the vast majority of operative embodiments fall within the scope of the claims. In regard to Splenhauer et al., applicant argues that the reference does not conclude lower detection limits of HIV using a reporter system.

Applicant's arguments, as well as a review of the reference, have been carefully considered, but are found unpersuasive. While it is agreed that claims can encompass non-enabling embodiments, it must also be evident that the limitations recited in the claim are enabled for the skilled artisan to practice the claimed invention without undue experimentation. Claim 43 recites that the method can detect "at least one HIV virus". Therefore, the detection of this single HIV virus by the instant method is a critical limitation in the claim because it is specifically recited. However, there is no evidence in the working examples or the prior art that suggests that the instant method is enabled for detecting the presence of one HIV virus.

In response to applicant's assertion regarding the teachings of Splenhauer et al., although the reference does not specifically "conclude" lower detection limits, this conclusion is evident in the data presented in Figure 2 on page 294. If less than 0.03 to 0.12 $TCID_{50}$ were detected by the assay system of Splenhauer et al., this data would be apparent in Figure 2. However, Splenhauer et al. do not observe a signal with a sample comprising less than 0.03 $TCID_{50}$ and Splenhauer et al. is acutely interested in measuring the quantity of HIV particles accurately. The disclosure does not present data that would indicate that the limitation of "at least one" recited in the claim is enabled.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 37-49 and 65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Littman et al. (US 6,258,527) and Chackerian et al. (Journal of Virology. 1997; 71 (5): 3932-3939).

Applicant argues that neither Littman et al. nor Chackerian et al. anticipate the claim limitations and do not provide motivation to express all of the receptors recited in the claim or to detect HIV using a cell line expressing all three receptors.

In response, the lack of anticipation of the claims by Littman et al. or Chackerian et al. is acknowledged in the previous Office action as the rejection is under 35 USC § 103. Further, it is noted that applicant is arguing the reference individually. One cannot show nonobviousness by

attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant cites case law that discusses the two criteria required for analysis in the combining of references. Applicant also cites case law stating that merely because a combination can be achieved does not render it obvious without some suggestion of desirability from the prior art. Applicant specifically argues that there is no suggestion of desirability for a cell expressing the three receptors recited in either reference and no motivation to combine the two. Applicant argues that the disclosure prompted impermissible hindsight to combine the references. Applicant further argues that the instant invention offers unexpected results of being as susceptible to HIV infection as PBMC's, is able to detect low viral titers and detects a near-linear range of HIV titers.

Applicant's arguments as well as a review of the references have been carefully considered, but are found unpersuasive.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

In this case, Littman et al. teach a transformed that expresses CD4, CCR5 and a reporter gene or CD4, CXCR4 and a reporter gene. Littman et al. teach quantifying virus particles by the amount of reporter gene expression, see column 5, lines 5-20.

Chackerian et al. teach sMAGI cells expressing CD4 and CD5, or CD4 and CXCR4 receptors with a green fluorescent reporter protein, see the first paragraph under materials and methods and the "Construction..." section on page 3933 and the results section.

Although neither reference teach expressing CD4 and CCR5 and CXCR4 receptors in the same cell, one of ordinary skill in the art at the time the invention was made would have been motivated to express all three receptors, CD4 and CCR5 and CXCR4, in the same cell line to enable infection of any strain, type, or clade of HIV virus. Chackerian et al. teaches that cell lines expressing CD4 and CXCR4 are only susceptible to T-tropic HIV isolates, while cell lines expressing only CD4 and CD5 receptors are only susceptible to M-tropic HIV, see the discussion section. One of ordinary skill in the art at the time the invention was made would have been motivated to incorporate the CD4 and the HIV co-receptors to relieve infectivity blocks in cells deficient in the a required receptor. Both references teach motivation to express HIV co-receptors in cells that do not normally express the receptors to render the cells more susceptible

to HIV infection. It is clearly evident from the teachings of Chackerian et al. that cells only expressing CD4 and CCR5 are only susceptible to M-tropic HIV and cells only expressing CD4 and CXCR4 are only susceptible to T-tropic HIV. Therefore, to render a cell susceptible to M- and T-tropic viruses, it would have been prima facie obvious from the teachings in the references that all three HIV co-receptors are required to be expressed on a cell surface. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation for producing the claimed invention because it is taught by Littman et al. and Chackerian et al. which co-receptors are required for various types of HIV infection and how to co-express the different receptors in cells for successful viral infection.

With respect to arguments regarding unexpected results, both references teach cells comprising essential co-receptors required for HIV entry and infection. The patent office does not have facilities to perform comparisons between the materials. Therefore, since PBMC's express these same co-receptors, it is determined that the cells expressing the same combination of receptors taught by Littman et al. and Chackerian et al. would possess the same susceptibility to HIV infection as PBMC's. Further, both references are drawn to sensitive assays to quantitate "low viral titer". Therefore, the linear range of detection would not be unexpected as the reporter system of Littman et al. and Chackerian et al. amplifies with respect to the HIV titer present. Therefore, the invention as a whole would have bee prima facie obvious to one of ordinary skill in the art, absent unexpected results to the contrary.

In conclusion, the Office has met all of the criteria required to establish prima facie obviousness. The combination of references teach all of the limitations recited by the claims and

provide motivation for the ordinary artisan to combine the references with a more than reasonable degree of success.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon Foley whose telephone number is (703) 308-3983. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (703) 308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4426 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Shanon Foley
March 22, 2003

JAMES HOUSEL 3/23/03
SUPERVISORY PATENT EXAMINER
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